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EXAMINER

MEHTA, ASHWIN D

ART UNIT

PAPER NUMBER

1638

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s)

09/696,600

Applicant(s)

PETERSON ET AL.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 11-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 18-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 January 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application). *However, see page 2.*
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. The substitute drawings submitted 21 January 2003, in response to form PTO-948, have been approved by the Draftsperson.
3. The objections to claims 6, 7, 9, 20, 22, and 23 are withdrawn, in light of the claim amendments.
4. The rejection of claims 18, 19, and 21 under 35 U.S.C. 112, 2nd paragraph, is withdrawn in light of the claim amendments.

Election/Restrictions

5. Applicants are reminded that non-elected claims 11-17 are still pending and require cancellation.

Priority

6. Applicants are reminded that the claim for domestic priority to provisional application 60/069,057 has been denied, as the instant application was filed more than one year after the filing of the provisional.

Claim Rejections - 35 USC § 112

7. Claims 1-10, 20, and 22-35 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record stated in the Office action mailed 16 October 2002 under item 5. Applicants traverse the rejection in the paper filed 10 March 2003. Applicants' arguments have been fully considered but were not found persuasive.

In claims 1, 5, and 8: the claims were rendered indefinite because of the recitation "making available to the plant a transposase". Applicants amended the claims to recite, "introducing a transposase to the plant." However, it is not clear what is meant by the recitation, as the transposase must be within the plant. It is again suggested that the recitation recite -- expressing a transposase within the plant--.

In the previous Office action, claim 8 was rejected as being indefinite for several reasons, making the claim confusing (Office action mailed 16 October 2002, paragraph bridging pages 4-5). Applicants amended the claim. However, the recitation "having homologous regions to a fragment of a gene" in lines 2-3 still renders the claim indefinite. The recitation indicates that only the coding sequences for a fragment of a gene are present, which indicates that a whole gene would not be generated upon recombination. This is not consistent with the last line of the claim, which recites "and subsequent transcription of said gene".

Claim 20 was rejected because it was not clear what was meant by "a maize recombination construct of claim 18 in a plant". Applicants have amended the claim. However, the recitation "in a plant transformed with said construct" still renders the claim indefinite. It is

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not clear what is meant by the recitation "in a plant". Further, there is insufficient antecedent basis for "said construct".

Claims 19, 20, 22, and 23 were rejected because the recitation "composition of matter" was not clear, making the metes and bounds of the claim unclear. Applicants argue that the amendment to the claims more clearly show what is encompassed by "composition of matter" (response, page 11, 1st full paragraph). However, the claim amendments do not address the recitation, and do not further make clear what is encompassed by the recitation. Further, as the compositions of matter are not clear, it is not clear what is undergoing homologous recombination. Further still, because the nature of the composition of matter is not clear, it is also not clear what is meant by "introduction of a maize transposase" in line 2 of claims 19 and 20.

8. Claims 1-10 and 18-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the claim is indefinite because it does not indicate what is being induced to homologously recombine. A recombination construct and transposase are "introduced to the plant", but this does not indicate what is undergoing homologous recombination.

In claims 1, 5, 8: the recitation "introducing a recombination construct to the plant" in claims 1, "introducing to the plant" in claims 5 and 8 render the claims indefinite. It is not clear what is meant by the recitation, as it does not exactly indicate that the construct is within the

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plant as a result of the introduction. It is suggested that the claims be amended to indicate that the constructs are introduced --into-- the plant.

In claims 6, 9, 25, 33, and 35: the claims are indefinite because they employ improper Markush terminology. The term "and" in line 3 of the claims should be deleted.

In claims 18-20: the recitation "which can be induced to undergo homologous recombination" renders the claim indefinite. It is not clear what is meant by an entire construct, or an entire composition of matter, undergoing recombination. It is suggested that the claims be amended to indicate that it is the direct repeats that undergo recombination, as this is what is taught by the specification.

In claim 19: the recitation "as part of a vector" in the last line renders the claim indefinite. It is not clear whether the recitation is limiting the composition of matter to being a vector. The metes and bounds of the claims are not clear.

In claims 19, 20, and 24: the recitation "agronomically significant gene" renders the claims indefinite. It is not exactly clear what types of genes are encompassed by this recitation.

In claim 22: the recitation "which further comprises a gene internal to said direct repeat sequences" renders the claim indefinite. Parent claim 20 indicates that an agronomically significant gene is internal to the direct repeats. It is not clear if the gene mentioned in claim 22 is the same as, or in addition to, the gene in claim 20.

9. Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

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the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards a method to induce homologous recombination in a plant comprising introducing to the plant a maize Ds element containing overlapping sequences having homologous regions to a fragment of a gene, and introducing a transposase, so as to induce homologous recombination and subsequence transcription of said gene.

The specification teaches the construction of a plasmid, termed "GU-Ds-US," comprising a Dissociation (Ds) element flanked by 2 partially overlapping non-functional segments of the GUS coding sequence (Example 1, Figure 1). The plasmid was introduced into Arabidopsis plants via vacuum infiltration. T1 seed were harvested from the transformed plants. T2 seeds were collected from those plants that had single insertions of the plasmid, and put on selection plates to obtain homozygous lines. Pollen from these lines was crossed to plants expressing Ac transposase or to wild-type plants. F1 heterozygous seeds were planted, and stained for GUS at the full rosette stage. Control plants showed few blue sectors, plants with both the plasmid and Ac showed, hundreds (Example 3). The structure of the GU-Ds-US transgene in the presence and absence of Ac was determined using PCR. A band predicted to arise from Ds excision followed by recombination between the overlapping GUS segments was found only in those plants containing both GU-Ds-US and expressing Ac (Example 4).

However, the specification does not teach homologous recombination of overlapping sequences of gene fragments within a Ds element, as encompassed by claim 8. As discussed above, the specification teaches that the recombination events occur between homologous sequences comprising overlapping sequences of the GUS gene that flank the Ds element, and

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that the recombination occurs after Ds excision. Examples of recombination between nucleotide sequences occurring within Ds elements, while within a plant genome, *in vitro*, or within plant cells following excision from the genome, are lacking in the prior art. In the absence of further guidance, undue experimentation would be required by one skilled in the art to use the claimed method to induce recombination between sequences within the Ds element. See also Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art, and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

10. Claims 1-4, 27, and 32 remain rejected under 35 U.S.C. 102(b) as being anticipated by Shalev et al. (Genetics, July 1997, Vol. 146, pages 1143-1151), for the reasons of record stated in the Office action mailed 16 October 2002 under item 6. Applicants traverse the rejection in the paper filed 10 March 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that there is no excision of the Ac element from the claimed construct, whereas Shalev's assay finds that the excision of Ac induces recombination between nonallelic sequences (response, page 11, last paragraph). However, the claims do not place any restriction at all on the sequences that undergo recombination. The only limitations in claim 1 are that a

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recombination construct and a transposase are introduced into a plant. The limitations introduced by the other claims are encompassed by teachings of the reference.

Claim Rejections - 35 USC § 103

10. Claims 1-7, 24-29, 31, and 32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Swoboda et al. (EMBO, 1994, Vol. 13, pages 484-489) in view of Shalev et al. (Genetics, July 1997, Vol. 146, pages 1143-1151), Holtorf et al. (Plant Mol. Biol., 1995, Vol. 29, pages 637-646), Hain et al. (Nature, 1993, Vol. 361, pages 153-156), and Fromm et al. (Biotechnology, 1990, vol. 8, pages 833-839), for the reasons of record stated in the Office action mailed 16 October 2002 under item 7. Applicants traverse the rejection in the paper filed 10 March 2003. Applicants' arguments have been fully considered but were not found fully persuasive.

Applicants reiterate the statement made by the Examiner in the last Office action concerning what Swoboda et al. do not teach (response, page 12, 2nd full paragraph). However, Applicants are not considering the teachings of the other references. By concentrating on this one statement, Applicants ignore the combination of the references, and the remainder of the rejection. Applicants next turn their attention to Shalev et al., again arguing that there is no excision of the Ac element from the claimed constructs (response, page 12, 3rd full paragraph). However, the claims do not include any recitation indicating the events the cause the recombination event. The method of claim 1 only requires the introduction of any recombination construct and any transposase in a plant. The claim does not even indicate what sequences are undergoing recombination. Claim 5 indicates the recombination construct has homologous

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regions that recombine to result in a functional gene upon introduction of a transposase. The claim does not place any limitations on what other events are to occur. None of the other method claims place any limitations as to what may not be present in the recombination construct, nor on the events that can or cannot occur. Applicants argue that Holtorf et al. merely teach heat shock promoters, and do not suggest including the Ac transposase coding sequence on the recombination construct under the control of an inducible promoter (response, paragraph bridging pages 13-14). However, a reference does not need to actually suggest changes or possible improvements. *In re Sheckler*, 438 F.2d 999,1001; 168 USPQ 716, 717 (CCPA 1971). Further, it is presumed that persons of ordinary skill in the art have a level of knowledge apart from the content of the references, and a conclusion of obviousness can be reached from common knowledge or common sense without any specific hint or suggestion in a particular reference. See *In re Bode*, 550 F.2d 656,660, 193 USPQ 12, 16 (CCPA 1977); *In re Jacoby*, 309 F.3d 513, 516, 135 USPQ 317, 319 (CCPA 1962); *In re Bozek*, 416, F.2d 1385, 1390, 163 USPQ 545, 549 (CCPA 1969). Holtorf et al. teach experiments that compared expression patterns of transgenes operably linked to different promoters. It was common sense that any transgene of choice could have been linked to the heat shock promoter taught by the reference. The reference did not need to list each and every gene of interest known in the prior art. Applicants argue that Hain et al. merely teach enhanced disease resistance conferred by a grape stilbene synthase gene (response, page 13, 1st full paragraph). However, this reference was only cited as a source of a disease resistance gene, to address those claims that limit the type of gene to be used. Applicants argue that Fromm et al. merely teaches the production of transgenic maize plants (response, page 13, 2nd full paragraph). However, this reference was cited to indicate a method to transform

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maize plants was known in the prior art, to address those claims that limit the type of plant that is to be used with the method.

Applicants also argue that Shalev teaches that GUS reactivation only occurs with Ac in 3'ΔGUS x 5'ΔGUS: Ac crosses, but not with the Ds element, while Applicants' invention is directed to the finding that overlapping foreign gene sequences containing a maize Ds element can be induced to undergo homologous recombination upon introduction of the Ac transposase (response, paragraph bridging pages 13-14). Applicants' argument was found persuasive to withdraw the rejection from claims 8-10, 18-23, and 30. However, claims 1-4 do not mention anything about overlapping sequences, Ac transposase, and claim 1 does not mention Ds. There is no requirement in these claims that the overlapping sequences flank the Ds element, or that the Ds element is to be excised in order for the recombination event to take place. Claim 5 does not mention Ds.

11. Claims 1-10 and 18-35 remain rejected.

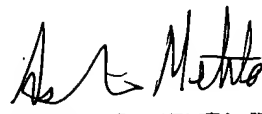
Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular

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communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

May 21, 2003


ASHWIN D. MEHTA, PH.D
PATENT EXAMINER